High-Frequency Hippocampal Oscillations Activated by Optogenetic Stimulation of Transplanted Human ESC-Derived Neurons.

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Public Summary:
Human embryonic stem cell (hESC) based neural transplantation is a potential therapeutic option for many neurodegenerative disorders, including Parkinson's disease and Alzheimer's disease. However, it has been unclear whether a massive number of transplanted hESCs-derived neurons can actually integrate and communicate with existing neural networks composed of endogenous neurons in the host brain. In this work we showed for the first time that neurons derived from hESCs are capable of integrating and functionally communicating with the neurons in the host brain after transplantation. For this we engineered hESCs to produce neurons that express certain proteins which can respond to specific wave lengths of light that excite them. When these neurons are excited, they produce electrical activity which they transmit to other neurons to which they are connected. Using this system, we we were able to measure electrical activity in the host neurons (which do not express the light-responsive protein) in response to light stimulation on the transplanted neurons derived from stem cells. This result proved that the transplanted neurons were capable of transmitting activity to the host neural networks.

Scientific Abstract:
After transplantation, individual stem cell-derived neurons can functionally integrate into the host CNS; however, evidence that neurons derived from transplanted human embryonic stem cells (hESCs) can drive endogenous neuronal network activity in CNS tissue is still lacking. Here, using multielectrode array recordings, we report activation of high-frequency oscillations in the beta and gamma ranges (10-100 Hz) in the host hippocampal network via targeted optogenetic stimulation of transplanted hESC-derived neurons.